

REMARKS

The comment in the Office Action regarding claims 50-54 not reading on the elected species is not understood. Applicants' Reply of July 21, 2003 did not list these claims as reading on the elected species. Applicants concur with the Examiner that they do not read on the elected species.

The rejection of claims 11 and 12 under 35 U.S.C. §112, second paragraph is believed overcome by the foregoing amendments. The claimed invention is directed to a mixture of at least two different salts of the same active ingredient having different solubilities. Original claims 11 and 12 were confusing in that they appeared to read on a single salt. Accordingly, the claims have been amended to clearly conform to the salt mixture recited in the parent claim. The Examiner's assistance in pointing out this confusion in the claims is acknowledged with appreciation.

The Office Action indicates that claims 1-67 were rejected under 35 U.S.C. §112, 1st paragraph, for alleged lack of enablement. However, since claims 10, 13, 14, 16, 19, 20, 22-29, 33-54 and 59-61 have been withdrawn from consideration, the rejection is presumed to apply only to claims 1-9, 11, 12, 15, 17, 18, 21, 30-32, 55-58 and 62-67, which are under examination. In any event, the rejection is respectfully traversed.

The rejection is predicated on the fact that the invention claims a broad range of salts of salt-forming pharmaceutically active agents. Applicants note that the concept of salt-formation is not unpredictable. On the contrary, it is well known that pharmaceutically active agents with basic groups, such as amino functions, will form salts with acids. Moreover, it is not unpredictable that salts of pharmaceutically active agents with different anions will have different solubilities. This is true over the broad range of pharmaceutically active agents and does not in any way vary or depend upon the particular pharmaceutical activity of the agent.

Furthermore, the description provides explicit guidance for:

- Salt formation (page 3, lines 12-17);
- A list of compounds for salt formation with the active substance (page 5, line 28 to page 6, line 5 and page 6, lines 18-23)
- A method for determining the water solubility of a salt of an active substance (page 17, lines 13-31);
- A method for preparing a dosage form of the active ingredient salts (page 14, line 28 to page 15, line 26);
- A method for applying a protective coating in cases where the acidic component of the salt is a weaker acid than the hydrochloric acid in the stomach (page 10, line 32 to page 11, line 32); and
- A process for applying coatings (page 12, lines 9-29 and page 15, line 28 to page 16, line 19).

Inasmuch as none of these aspects of the claimed invention is unpredictable, applicants submit that a person of ordinary skill in the art guided by the teachings of the specification would be able to make and use the claimed invention as broadly as claimed.

Pointedly, the Office Action does not explain why a person skilled in the art would be unable to make or use salts of any of the pharmaceutically active ingredients embraced by the claim, nor does the Office Action give any example of a pharmaceutically active agent embraced by the claim with which a person of ordinary skill in the art would be unable to practice the invention. Again, applicants point out that because the phenomenon of the invention does not depend on the particular pharmaceutical activity of the active ingredient, the fact that the claim embraces agents with a broad variety of pharmaceutical activities is irrelevant. Salt formation is not unpredictable, and the teachings and examples of the specification are sufficient to demonstrate the effectiveness of the claimed invention over the entire range of claimed salt-forming pharmaceutically active agents. In the absence of any explanation of a reason why a person of ordinary skill in the pharmaceutical art would not be able to

make and use salt mixtures as claimed, the statements in the disclosure must be considered enabling, and the rejection cannot stand. In re Marzocchi 169 USPQ 367 (CCPA 1971). Reconsideration and withdrawal of the rejection are therefore respectfully requested.

The rejection of claims 1-9, 11, 12, 15, 17, 18, 21, 30-32, 55-58 and 62-67 as obvious over Oshlack et al., WO 99/01111 is also respectfully traversed. Oshlack et al. disclose sustained release oral solid dosage forms of various pharmaceutically active agents, including salts. However, Oshlack et al. does not disclose or suggest in any ways using a mixture of two different salts of the same pharmaceutically active ingredient having different solubilities as claimed.

The rejection cites to decisions holding it *prima facie* obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose. However true this may be regarding mixtures of two different pharmaceutically active agents, the logic breaks down and is not applicable to mixtures of two different salts of the same active agent as claimed in the present invention. The record is devoid of any example of such a mixture, and with good reason. The formation of a mixture of two different salts of the same active ingredient is unquestionably more troublesome and inconvenient than the provision of a single salt. There is nothing in the record which would lead a person of skill in the art to expect any advantage from using a mixture of two materials over using a single material when there is only one active ingredient present in the mixture. All that the prior art would lead a person of ordinary skill in the art to expect would be that such a mixture of salts of the same active ingredient would have the same effect as a single salt of the active ingredient. Thus, the prior art gives a person of ordinary skill in the art no reason or motivation to form such a mixture of salts of the same active ingredient having different solubilities. Accordingly, it cannot be fairly be said to be obvious for a person of ordinary skill to incur the trouble and inconvenience of forming such a mixture for no reason.

It is only the applicants who have recognized that unexpected advantages of extended activity could be attained from using a mixture of at least two different salts of the same active ingredient having different solubilities as claimed in the present invention. Consequently, it is only after a consideration of the applicant's disclosure that there is any reason or motivation to form such a mixture. However, such hindsight consideration is clearly improper.

Prior cases dealing with mixtures of different active agents known to be useful for the same purpose are inapposite because their facts are different. Two different active agents can be presumed to have some differences in activity so that the combination would yield a broadened spectrum of activity. The same is **not** true for two different salts of the same active ingredient. Consequently, the reasoning of cases dealing with combinations of two different active agents is not applicable to the present invention, which deals with a combination of at least two different salts of the same active agent having different solubilities.

Obviousness is not susceptible of determination by rote application of mechanical rules derived from cases with different facts. Rather obviousness in any given case must be decided on the facts of that case. *In re Jones* 21 USPQ2d 1941 (Fed. Cir. 1992) ("Every case, particularly those raising the issue of obviousness under section 103, must necessarily be decided upon its own facts."); *Ex parte Goldgaber* 41 USPQ2d 1172 (B.P.A.I. 1995) ("Again, each case under 35 USC 103 must be decided on its own particular facts.") Under the facts of this case, since the state of the art provides no motivation to make a combination of at least two different salts of the same active ingredient having different solubilities as claimed, the obviousness rejection is not well founded. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the foregoing amendments and remarks, the application is respectfully submitted to be in condition for allowance, and prompt, favorable action thereon is earnestly solicited.



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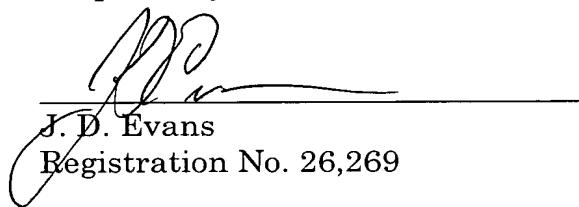
Reply to Office Action

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned at (202) 624-2845 would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #02931050986).

Respectfully submitted,

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